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L1: Entry 8 of 20

File: USPT

Dec 26, 2000

DOCUMENT-IDENTIFIER: US 6165713 A

TITLE: Composition and methods relating to DNA mismatch repair genes

Other Reference Publication (40):

Sean Baker et al., "Male Mice Defective in the DNA Mismatch Repair Gene PMS2 Exhibit Abnormal Chromosome Synapsis in Meiosis," Cell, Jul. 28, 1995, vol. 82, No. 2, pp. 309-319.

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L3: Entry 1 of 1

File: USPT

Nov 14, 2000

US-PAT-NO: 6146894

DOCUMENT-IDENTIFIER: US 6146894 A

TITLE: Method for generating hypermutable organisms

DATE-ISSUED: November 14, 2000

INVENTOR - INFORMATION

NAME	CITY	STATE	ZIP CCDE	COUNTRY
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Kinzler; Kenneth W.	BelAir	MD		

US-CL-CURRENT: 435/440; 435/325, 435/455

CLAIMS:

We claim:

1. A method of making a mammalian hypermutable cell, comprising the step of: introducing into a mammalian cell a polynucleotide comprising a dominant negative allele of the mismatch repair gene, PMS2, whereby the cell becomes hypermutable.
2. The method of claim 1 wherein the polynucleotide is introduced by transfection of a suspension of cells in vitro.
3. The method of claim 1 wherein the mismatch repair gene is human PMS2.
4. The method of claim 3 wherein the allele comprises a truncation mutation.
5. The method of claim 3 wherein the allele comprises a truncation mutation at codon 134 as shown in SEQ ID NO: 1.
6. The method of claim 5 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type PMS2 as shown in SEQ ID NO: 1.
7. A homogeneous composition of cultured, hypermutable, mammalian cells which comprise a dominant negative allele of the mismatch repair gene, PMS2.
8. The homogenous composition of claim 7 wherein the mismatch repair gene is human PMS2.
9. The homogeneous composition of claim 7 wherein the cells express a protein consisting of the first 133 amino acids of human PMS2 which functions as a dominant-negative protein.
10. The homogeneous composition of claim 7 wherein the cells express a protein consisting of the first 133 amino acids of PMS2 which functions as a dominant-negative protein.
11. A method of generating a mutation in a gene of interest comprising the steps of: growing a population of mammalian cells comprising the gene of interest and a dominant negative allele of the mismatch repair gene PMS2, wherein the cell is hypermutable; identifying a cell wherein the gene of interest harbors a mutation.

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US-CL-CURRENT: 435/440; 435/325, 435/455APPL-NO: 9/ 059461 [PALM]

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